

Fig. 1

3D structure topology

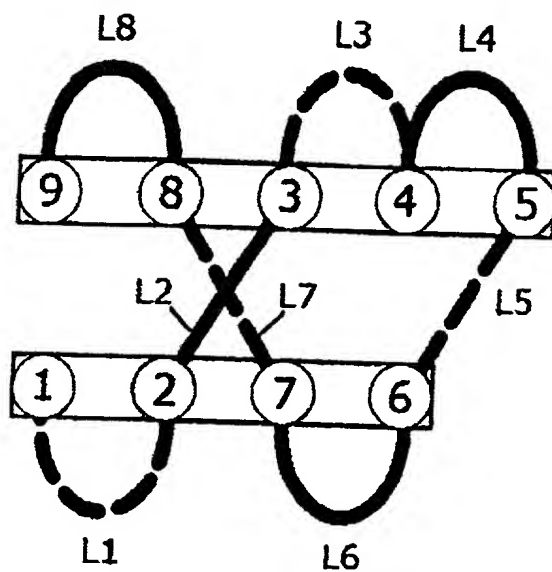
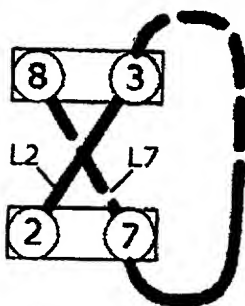


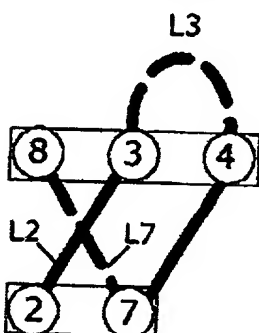
Fig. 2

Structural Deviations

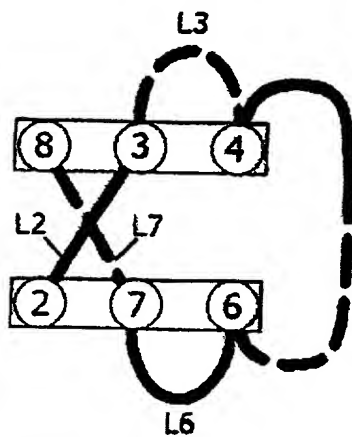
4 beta elements:



5 beta elements:

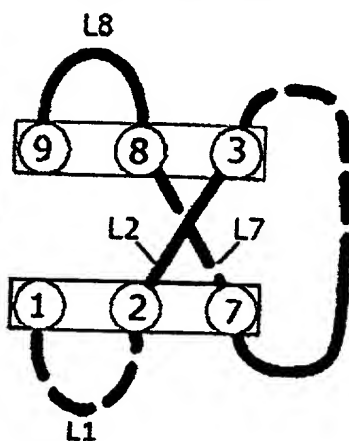


6 beta elements-a:



1GOY: Interleukin-1
 receptor type 1

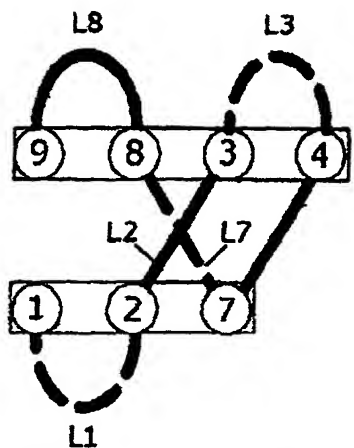
6 beta elements-b:



1J88: Fc epsilon receptor
 type alpha

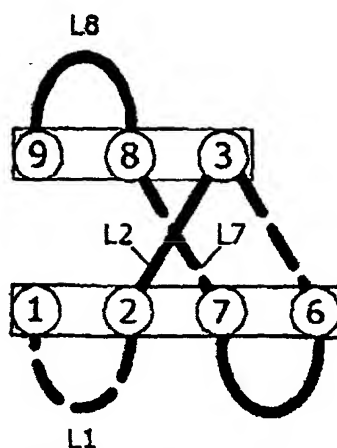
Fig. 3a

7 beta elements-a:



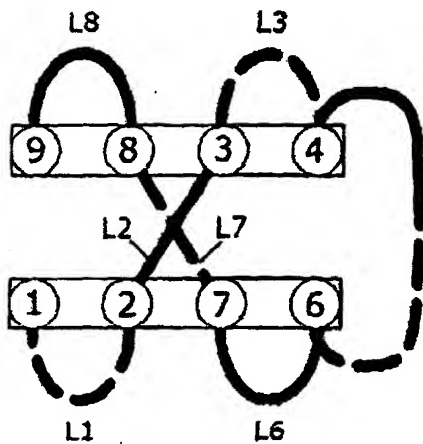
2DL1: Immunoglobulin killer
 receptor 2dl2

7 beta elements-b:



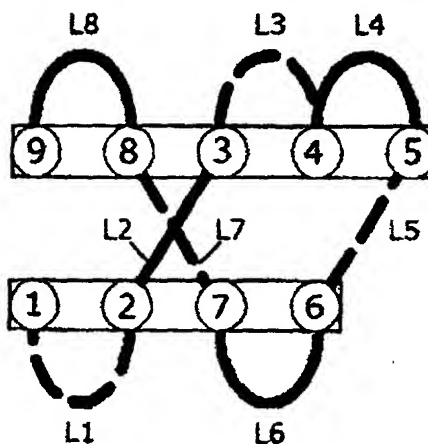
1FF5: E-cadherin domain

8 beta elements:



1IAR: Interleukin-4 alpha receptor

9 beta elements:



All antibody and T-cell receptor
 variable domains

Fig. 3b

Modular Affinity & Scaffold Transfer (MAST) Te

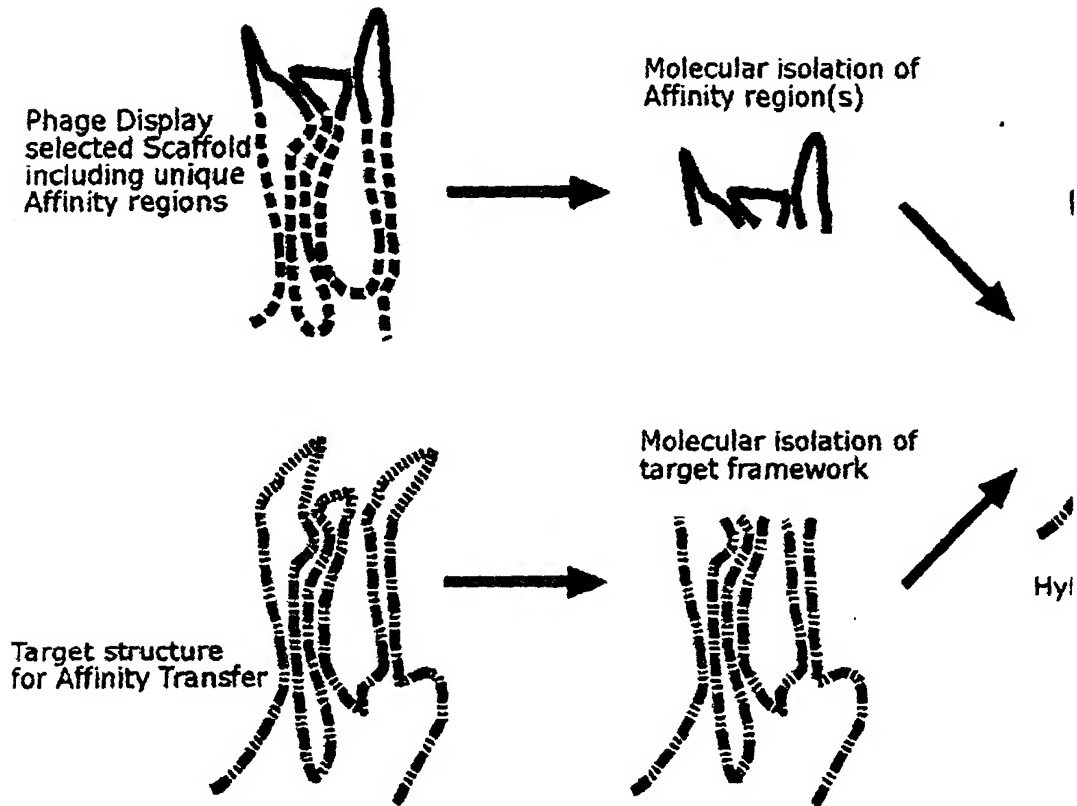


Fig. 4

STRUCTURAL ALIGNMENT: EXAMPLES OF 1F2X V_H CAMELID ANTIBODY VARIABLE FRAGMENT

	1	2	3	4	5	6	7	8	9
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---vstycmchfrq-APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLQMNSL-K-PEDTAI	LYYCAGSTVASTGWC	SLRPYDHYHRCGGTQ-VTVS				
1QD0	QVQLQOE-SG--G-GLVQAGGSLRLSCAASGYS	---asghghyGNGWFRQ-VPGK--EREFVAATIRWAG--	KETWYKOSVKGRTTISODNAKNTVYLQMNSL-K-GEDTAI	LYYCAGSTVASTGWC	SLRPYDHYHRCGGTQ-VTVS				
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---vstycmchfrq-APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLQMNSL-K-PEDTAI	LYYCAGSTVASTGWC	SLRPYDHYHRCGGTQ-VTVS				
8FAB	AVKLIVQ-AG--G-GVQVQAGGSLRLSCAASGYS	---ISNYGCHWYRQ-APGK--GJENWAVIN--Yng	STTIGOSVKGRTTISODNAKNTVYLQMNSL-K-PEDTAI	LYYCAGSTVASTGWC	SLRPYDHYHRCGGTQ-VTVS				
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---vstycmchfrq-APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLQMNSL-K-PEDTAI	LYYCAGSTVASTGWC	SLRPYDHYHRCGGTQ-VTVS				
1VSC	-FKTET-TPesR-YLAQIGSVSLTCTGCE	---SPEFSIRIVY-Id-----	spLNGAVTMEG--TTSTLTMMNPV-S-PGNEHSY	CTATICE-----	SKLEK-GIQ-VELY				
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---vstycmchfrq-APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLQMNSL-K-PEDTAI	LYYCAGSTVASTGWC	SLRPYDHYHRCGGTQ-VTVS				
1N3	LGSLFLA-TC--v-----	---NGVCEVTVWg-----	asgsktlagp-k-----	GPITg-----					
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---vstycmchfrq-APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLQMNSL-K-PEDTAI	LYYCAGSTVASTGWC	SLRPYDHYHRCGGTQ-VTVS				
1F97	KGSVYT-AGS-B-VQVPENISIKTCTYSGTS	---SPRVEKKEV-Q-GS--TTALVCYMS-----	QITAPYADRVTFSS-----	SGITFSSV-I-RKDNCEVT	CMVSEEGG-----				
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---vstycmchfrq-APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLQMNSL-K-PEDTAI	LYYCAGSTVASTGWC	SLRPYDHYHRCGGTQ-VTVS				
1ENF	VPPFTD-LR--IHLIGP--DTWRVTNAPPPS	---IDLTFELVRSYpKRE--EDVRELSIS-----							
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---vstycmchfrq-APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLQMNSL-K-PEDTAI	LYYCAGSTVASTGWC	SLRPYDHYHRCGGTQ-VTVS				
1CEB	QNAFKLGI-I-CQAD--XAEIHWEOGdn	---ISPLIHYTIQEN--SFTpaSDAYEAV-----							
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---vstycmchfrq-APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLQMNSL-K-PEDTAI	LYYCAGSTVASTGWC	SLRPYDHYHRCGGTQ-VTVS				
1IAR	IEPGLN-LVnt-----	---NVSDTLLITWSNFPYppdnYlnHLTYAVNISE--NDPA--DEFRIYNY-----							
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---vstycmchfrq-APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLQMNSL-K-PEDTAI	LYYCAGSTVASTGWC	SLRPYDHYHRCGGTQ-VTVS				
1F4H	IQQFRI-SG-----	---QTIEVTsey-lfrhndNELLHWYA-LDg-----	IPLASGRYP--ld--v-----						

Figure elements explained:

Underlined domains represent (putative) beta-elements 1-9
Capital letters indicate conserved structural amino acids
~ indicate the absence of amino acid residues

Aligned protein domains from:

- 1F2X Single domain camelid antibody Cab-Ca05
- 1QD0 Camelid heavy chain variable domain
- 8FAB Heavy chain from human Iggl
- 1VSC Human Vcam-1
- 1NS3 Structure Of Hcv Protease (Bk Strain) from hepatitis C-virus
- 1F97 Soluble Part Of The Junction Adhesion Molecule From Mouse
- 1CFB Fragment Of Human Fibronectin Encompassing Type-III Repeats 7 Through 10
- 1IAR Drosophila neuroglian
- 1IAR Human Interleukin-4 receptor alpha chain complex
- 1F4H E. Coli (Lacz) Beta-Galactosidase (Orthorhombic)

Fig. 5

Scaffold with V_{HH} 1MEL CDR regions

N V K L V E K G G N F V E N D D D L K L
AATGTGAAACTGGTTGAAAAAGGTGGCAATTCGTGCGAAAACGATGACGATCTTAAGCTC
T C R A E G Y T I G P Y C M G W F R Q A
ACGTGCCGTGCTGAAGGTTACACCATTGGCCCGTACTGCATGGGTTGGTTCCGTCAGGCG
P N D D S T N V A T I N M G G G I T Y Y
CCGAACGACGACGACTACTAACGTGGCCACGATCAACATGGGTGGCGGTATTACGTACTAC
G D S V K E R F D I R R D N A S N T V T
GGTGACTCCGTCAAAGAGCGCTTCGATATCCGTGCGGACAACGCGTCCAACACCGTTACC
L S M D D L Q P E D S A E Y N C A G D S
TTATCGATGGACGATCTGCAACCGGAAGACTCTGCAGAATACAATTGTGCAGGTGATTCT
T I Y A S Y Y E C G H G L S T G G Y G Y
ACCATTTACGCGAGCTATTATGAATGTGGTCATGGCCTGAGTACCGGCGGTACGGCTAC
D S H Y R G Q G T D V T V S S
GATAGCCACTACCGTGGTCAGGGTACCGACGTTACCGTCTCGTCG

Scaffold with V_{HH} 1BZQ CDR regions

N V K L V E K G G N F V E N D D D L K L
AATGTGAAACTGGTTGAAAAAGGTGGCAATTCGTGCGAAAACGATGACGATCTTAAGCTC
T C R A S G Y A Y T Y I Y M G W F R Q A
ACGTGCCGTGCTAGCGGTTACGCCTACACGTATATCTACATGGGTTGGTTCCGTCAGGCG
P N D D S T N V A T I D S G G G G T L Y
CCGAACGACGACGACTACTAACGTGGCCACCATCGACTCGGGTGGCGGGGTACCGTGTAC
G D S V K E R F D I R R D K G S N T V T
GGTGACTCCGTCAAAGAGCGCTTCGATATCCGTGCGGACAAGGCTCCAACACCGTTACC
L S M D D L Q P E D S A E Y N C A A G G
TTATCGATGGACGATCTGCAACCGGAAGACTCTGCAGAATACAATTGTGCAGCGGGTGGC
Y E L R D R T Y G Q R G Q G T D V T V S
TACGAACCTGCGCGACCGCACCTACGGTCAGCGTGGTCAGGGTACCGACGTTACCGTCTCG
S
TCG

Scaffold with V_{HH} 1HCV CDR regions

N V K L V E K G G N F V E N D D D L K L
AATGTGAAACTGGTTGAAAAAGGTGGCAATTCGTGCGAAAACGATGACGATCTTAAGCTC
T C R A E G R T G S T Y D M G W F R Q A
ACGTGCCGTGCTGAAGGTCGTACGGGTTCCGACCTACGATATGGGTTGGTTCCGTCAGGCG
P N D D S T N V A T I N W D S A R T Y Y
CCGAACGACGACGACTACTAACGTGGCCACGATCAACTGGGATAGCGCCGTACGTACTAC
G D S V K E R F D I R R D N A S N T V T
GGTGACTCCGTCAAAGAGCGCTTCGATATCCGTGCGGACAATGCCTCCAACACCGTTACC
L S M D D L Q P E D S A E Y N C A G G E
TTATCGATGGACGATCTGCAACCGGAAGACTCTGCAGAATACAATTGTGCAGGTGGTGAA
G G T W D S R G Q G T D V T V S S
GGCGGCACCTGGGATAGCCGTGGTCAGGGTACCGACGTTACCGTCTCGTCG

Underlined regions indicate specific affinity regions.

The sequence of underlined regions in each panel represent respectively loop L2 (~CDR1 and AR1), L4 (~CDR2 and AR2) and L8 (~CDR3 and AR4).

Fig. 6a

Structural topology of a primary scaffold

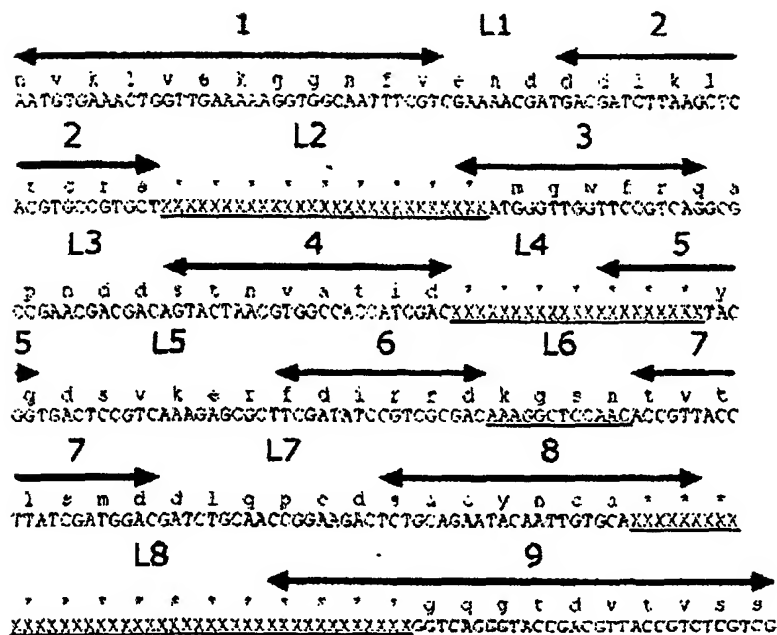


Fig. 6b